Paper No. 33

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ROBERT M. MORIARTY, RAJU A. PENMASTA, LIANG GUO, MUNAGALA S. RAO and RAJENDRA G. MEHTA

Appeal No. 09/008,957
Application No. 2004-0903

ON BRIEF

Before WINTERS, WILLIAM F. SMITH, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1.[1] Claim 1 is drawn to the compound 1α-hydroxyvitamin D_5, and a copy of that claim is appended to this decision.

[1] Claims 1-6 and 10-19 are pending and stand rejected under 35 U.S.C. § 103(a). Appellants have appealed only the rejection of claim 1.

The examiner relies upon the following references:

Holick et al. (Holick I)	4,728,643	March. 01, 1988
Holick et al. (Holick II)	5,254,538	Oct. 19, 1993
Gulbrandsen et al. (Gulbrandsen)	5,700,790	Dec. 23, 1997
Bishop et al. (Bishiop)	5,763,429	Jun. 9, 1998

Claim 1 stands rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holick I and II, Bishop and Gulbrandsen. After careful review of the record and consideration of the issue before us, we reverse.

PROCEDURAL BACKGROUND

The instant application was remanded by the Board to the examiner on September 8, 2003 for further consideration and analysis of specified evidence made of record by appellants. See Paper No. 31. Although the examiner did not expressly address the evidence specified in the remand,[2] in the interest of judicial economy and in the interest of advancing the prosecution of this application, the panel has determined that the issue is adequately before us on appeal, and has decided the merits of the appeal.

DISCUSSION

Claim 1 stands rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Holick I and II, Bishop and Gulbrandsen.

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[2] In the future, however, we suggest that upon remand of an application for further consideration and/or analysis of specified evidence, that the examiner expressly address each piece of evidence that may be listed in the remand by name.

Holick I and II, Bishop and Gulbrandsen are cited for teaching a generic group of vitamin D derivatives and their uses. According to the rejection, "[e]ach reference exemplifies 1α-hydroxyl-vitamin D_4 and/or 1α-hydroxyl-vitamin D_3." Supplemental Examiner's Answer, page 4.

The rejection concludes:

> The instant claim differs from the references by reciting a specific species not exemplified by the cited prior art. However, the cited prior art teach equivalence between hydrogen, methyl and or ethyl at C-24. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the present invention to select any of the species of the genus taught by the prior art, including 1α-hydroxyl-vitamin D_5 of the instant claim, because the ordinary artisan would have the reasonable expectation that any of the species of the prior art genus would have similar properties and, thus, the same uses as the prior art genus as a whole. The ordinary artisan would have been motivated to make additional compounds as taught by the cited prior art for use as taught by the prior art.

Id. at 5-6 (citations omitted).

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993) (citations omitted). "If a prima facie case is made in the first instance, and if the appellant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed." In re Hedges, 783 F.2d 1038, 1039, 228 USPQ 685, 686

(Fed. Cir. 1986) (citing In re Piasecki, 745 F.2d 1468, 1472, 223 USPQ 785, 788 (Fed. Cir. 1984)).

Appellants do not argue the prima facie case. See Appeal Brief, page 5. Rather, appellants argue that they "have rebutted the . . . prima facie case by submitting evidence that shows that 1α(OH)D_5 possesses key properties (antiproliferative activity and significantly lower calcemic activity compared to the closest prior art compounds) that would have been unexpected to a person of ordinary skill in the art at the time of the invention in view of the prior art." Id.

Appellants have submitted several declarations, including the declaration of Dr. Robert Moriarty (Moriarity declaration), see Paper No. 13, which was supported by the statistical analysis of Dr. Samad Hedeyat, also provided in declaration form (Hedeyat declaration), see Paper No. 21, in support of their assertion of unexpected results. See Appeal Brief, page 8. Appellants assert that:

> The data in the Moriarity declaration . . . shows that, between 1α(OH)D_5 and 1α(OH)D_4, two synthetic compounds, 1α(OH)D_5 is significantly less calcemic than 1α(OH)D_4. This is an important improvement in properties, because, unlike the other known vitamin D analogues, the desirable antiproliferative activity of 1α(OH)D_5 is not offset by undesirably high calcemic activity. No one, including Bishop, anticipated that 1α(OH)D_5 would have such a favorable combination of properties.

Id.

The examiner argues in response:

> that the data presented . . . is not unexpected because Bishop teaches that the compounds have a lower tendency or inability to

> cause the undesired side effects of hypercalcemia and/or hypercalcuria and thus, allows said compounds to be administered as antiproliferative agents etc. without significantly altering calcium metabolism. Therefore, the ordinary artisan would have the reasonable expectation that any of the compounds of the genus taught by the prior art would have these properties. The ordinary artisan would also have the reasonable expectation that the favorable properties (i.e. lower adverse hypercalcemic and/or hypercalcuria effects) as taught [by] [sic] Bishop would vary between compounds of the prior art genus. Therefore, applicant's data is not unexpected because it shows what the ordinary artisan would expect between prior art compounds.

Supplemental Examiner's Answer, pages 6-7 (citations omitted).

Appellants have presented data in the Moriarity declaration to demonstrate that "1α(OH) Vitamin D_5 is considerably less calcemic than its closest known analogs: 1α(OH) Vitamin D_3, 1α(OH) Vitamin D_4, and 1α, 25$(OH)_2$ Vitamin D_3, all run side-by-side in the same laboratory." Moriarity Declaration, ¶4. The examiner, however, does not point to any deficiencies in the data; nor does there appear to be a disagreement that 1α(OH) Vitamin D_3, 1α(OH) Vitamin D_4, and 1α, 25$(OH)_2$ Vitamin D_3 are not the closest prior art compounds. Rather, the examiner relies on the following statements in Bishop to refute appellants' assertion of unexpected results.

According to Bishop:

> The 1α-hydroxyvitamin D compounds of formula (I) of the present invention are those that have effective antiproliferative and cell differentiation activity (i.e., reversal of malignant transformation), particularly with respect to cells of prostatic diseases, e.g., prostatic cancer and prostatic hyperplasia, but have a lower tendency or inability to cause the undesired side effects of hypercalcemia and/or hypercalcuria. In other words, the compounds of formula (I) can be administered at dosages that

> allow them to act as antiproliferative agents and cell differentiation agents when exposed to malignant or other hyperproliferative cells without significantly altering calcium metabolism. This selectivity and specificity of action makes the 1α-hydroxyvitamin D compounds of formula (I) useful and preferred agents for safely inhibiting hyperproliferation and promoting malignant or hyperplastic cell differentiation. The 1α-hydroxyvitamin D compounds of the present invention, thus, overcome the shortcomings of the known active vitamin D_3 compounds described above, and can be considered preferred agents for the control and treatment of malignant diseases such as prostate cancer as well as benign prostatic hyperplasia.

Id. at col. 5, line 60-col 6, line 13.

The above generic statement as to the properties of the compounds of Bishop, however, is insufficient to rebut appellants' declarations and data as to the unexpected properties of the claimed 1α-hydroxyvitamin D_5 compound, especially as the declaration compares the claimed 1α-hydroxyvitamin D_5 compound to 1α-hydroxyvitamin D_4, one of the preferred compounds of Bishop. See Bishop, col. 6, line 40. Therefore, the preponderance of the evidence of record does not support the conclusion that the claimed 1α-hydroxyvitamin D_5 compound is obvious over the combination of Holick I and II, Bishop and Gulbrandsen, and the rejection of claim 1 over that combination is reversed.

CONCLUSION

Because the examiner has failed to sufficiently address and rebut appellants' evidence that the compound of claim 1 has unexpected properties, for the reasons set forth supra, the rejection of claim 1 under 35 U.S.C. § 103(a) is reversed.

REVERSED

Sherman D. Winters)
Administrative Patent Judge)
)
)
William F. Smith) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
Lora M. Green) INTERFERENCES
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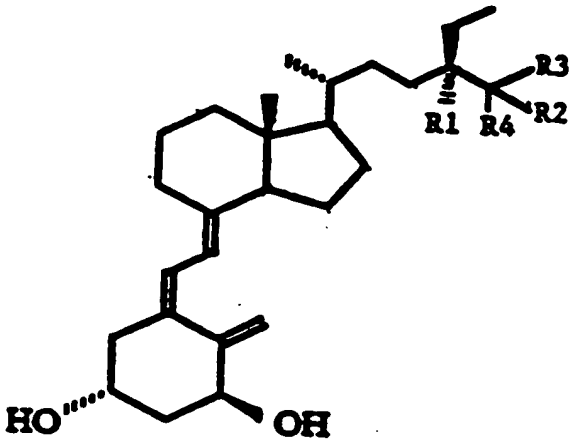
Appendix

1. A compound of formula I:



wherein:

R1 is hydrogen;

R2 is $-CH_3$;

R3 is $-CH_3$; and

R4 is hydrogen.